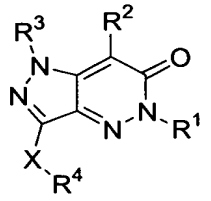
## CLAIMS

We claim:

1. A compound of formula **I**:



**I**

or a pharmaceutically acceptable salt or mixtures thereof,

wherein $R^1$ is selected from $-(L)_mR$, $-(L)_mAr^1$, or $-(L)_mCy^1$; L is an optionally substituted $C_{1-6}$ alkylidene chain wherein up to two non-adjacent methylene units of L are optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, $NRCO_2$, CO, $CO_2$, CONR, CSNR, OC(O)NR, $SO_2$, $SO_2NR$, $NRSO_2$, $NRSO_2NR$, C(O)C(O), or $C(O)CH_2C(O)$; m is 0 or 1; $Ar^1$ is an optionally substituted aryl group selected from a 3-8 membered monocyclic or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; and $Cy^1$ is an optionally substituted group selected from a 3-7-membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10-membered saturated or partially unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein $Ar^1$ and $Cy^1$ are each independently optionally substituted with up to five substituents selected from $Z\text{-}R^Y$; wherein Z is a bond or is a $C_1$-$C_6$ alkylidene chain wherein up to two non-adjacent methylene units of Z are optionally replaced by CO, $CO_2$, COCO, CONR, CSNR, OCONR, NRNR, NRNRCO, NRCO, NRCS, $NRCO_2$, NRCONR, NRCSNR, SO, $SO_2$, $NRSO_2$, $SO_2NR$, $NRSO_2NR$, O, S, or NR; and each occurrence of $R^Y$ is independently selected from R', halogen, $NO_2$, CN, OR', SR', $N(R')_2$, NR'C(O)R', NR'C(S)R', $NR'C(O)N(R')_2$, $NR'C(S)N(R')_2$, $NR'CO_2R'$, C(O)R', $CO_2R'$, OC(O)R', $C(O)N(R')_2$, $C(S)N(R')_2$, $OC(O)N(R')_2$, SOR', $SO_2R'$, $SO_2N(R')_2$, $NR'SO_2R'$, $NR'SO_2N(R')_2$, C(O)C(O)R', or $C(O)CH_2C(O)R'$;

$R^2$ is selected from halogen, $NO_2$, CN, -SR, $-N(R)_2$, $-(T)_nR$, or $-(T)_nAr^2$ wherein T is an optionally substituted $C_{1-4}$ alkylidene chain wherein up to two non-adjacent

methylene units of T are optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, $NRCO_2$, CO, $CO_2$, CONR, CSNR, OC(O)NR, $SO_2$, $SO_2NR$, $NRSO_2$, $NRSO_2NR$, C(O)C(O), or $C(O)CH_2C(O)$; n is 0 or 1; $Ar^2$ is an optionally substituted aryl group selected from a 5-6 membered monocyclic or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur wherein $Ar^2$ is independently optionally substituted with up to five substituents selected from $Q\text{-}R^X$; wherein Q is a bond or is a $C_1$-$C_6$ alkylidene chain wherein up to two non-adjacent methylene units of Q are optionally replaced by CO, $CO_2$, COCO, CONR, CSNR, OCONR, NRNR, NRNRCO, NRCO, NRCS, $NRCO_2$, NRCONR, NRCSNR, SO, $SO_2$, $NRSO_2$, $SO_2NR$, $NRSO_2NR$, O, S, or NR; and each occurrence of $R^X$ is independently selected from R', halogen, $NO_2$, CN, OR', SR', $N(R')_2$, NR'C(O)R', NR'C(S)R', $NR'C(O)N(R')_2$, $NR'C(S)N(R')_2$, $NR'CO_2R'$, C(O)R', $CO_2R'$, OC(O)R', $C(O)N(R')_2$, $C(S)N(R')_2$, $OC(O)N(R')_2$, SOR', $SO_2R'$, $SO_2N(R')_2$, $NR'SO_2R'$, $NR'SO_2N(R')_2$, C(O)C(O)R', or $C(O)CH_2C(O)R'$;

$R^3$ is hydrogen or an optionally substituted $C_{1-4}$ aliphatic group;

X is selected from a valence bond, O, S, or NR;

$R^4$ is selected from -R, $-(U)_jAr^3$, or $-(U)_jCy^3$; U is an optionally substituted $C_{1-6}$ alkylidene chain wherein up to two non-adjacent methylene units of U are optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, $NRCO_2$, CO, $CO_2$, CONR, CSNR, OC(O)NR, $SO_2$, $SO_2NR$, $NRSO_2$, $NRSO_2NR$, C(O)C(O), or $C(O)CH_2C(O)$; j is 0 or 1; $Ar^3$ is an optionally substituted aryl group selected from a 3-8 membered monocyclic or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; and $Cy^3$ is an optionally substituted group selected from a 3-7-membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10-membered saturated or partially unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein $Ar^3$ and $Cy^3$ are each independently optionally substituted with up to five substituents selected from $Y\text{-}R^Z$; wherein Y is a bond or is a $C_1$-$C_6$ alkylidene chain wherein up to two non-adjacent methylene units of Y are optionally replaced by CO, $CO_2$, COCO, CONR, CSNR, OCONR, NRNR, NRNRCO, NRCO, NRCS, $NRCO_2$, NRCONR, NRCSNR, SO, $SO_2$, $NRSO_2$, $SO_2NR$, $NRSO_2NR$, O, S, or NR; and each occurrence of $R^Z$ is independently selected from R', halogen, $NO_2$, CN, OR', SR', $N(R')_2$, NR'C(O)R', NR'C(S)R', $NR'C(O)N(R')_2$, $NR'C(S)N(R')_2$, $NR'CO_2R'$,

$C(O)R'$, $CO_2R'$, $OC(O)R'$, $C(O)N(R')_2$, $C(S)N(R')_2$, $OC(O)N(R')_2$, $SOR'$, $SO_2R'$, $SO_2N(R')_2$, $NR'SO_2R'$, $NR'SO_2N(R')_2$, $C(O)C(O)R'$, or $C(O)CH_2C(O)R'$; or

wherein $R^4$ and R, taken together with the nitrogen form an optionally substituted 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each occurrence of R is independently selected from hydrogen or an optionally substituted $C_{1-6}$ aliphatic group, or two R on the same nitrogen are taken together with the nitrogen to form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur; and

each occurrence of R' is independently selected from hydrogen or an optionally substituted group selected from $C_{1-6}$ aliphatic, $C_{6-10}$ aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 3-10 ring atoms, or wherein two R on the same nitrogen are taken together with the nitrogen to form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur,

provided that:

a) when X is NR; R, $R^3$, and $R^4$ are each hydrogen; $R^2$ is $-(T)_nR$ wherein n is 0 and R is hydrogen; and $R^1$ is $-(L)_mAr^1$ wherein m is 0; then $Ar^1$ is not:

i) 4-Cl or 4-OMe phenyl; or

ii) 3-$CF_3$ phenyl;

b) when X is NR; R and $R^3$ are each hydrogen; $R^2$ is $-(T)_nR$ wherein n is 0 and R is hydrogen; $R^4$ is 2-phenyl-4-quinazolinyl; and $R^1$ is $-(L)_mAr^1$ wherein m is 0; then $Ar^1$ is not:

i) phenyl, 3-OMe phenyl, 4-OMe phenyl, 2,4-diCl phenyl, 4-Cl phenyl, 3-$CF_3$ phenyl, or 4-OPh phenyl;

c) when X is NR; R and $R^3$ are each hydrogen; $R^2$ is $-(T)_nR$ wherein n is 0 and R is hydrogen; $R^4$ is 2-(2-trifluoromethyl-phenyl)-4-quinazolinyl; and $R^1$ is $-(L)_mAr^1$ wherein m is 0; then $Ar^1$ is not phenyl.

d) when X is a valence bond; $R^4$ is hydrogen; $R^3$ is $CH_3$; $R^2$ is either chloro or hydrogen; and $R^1$ is $-(L)_mAr^1$ wherein m is 0, then $Ar^1$ is not 3-trifluoromethyl phenyl or 2-fluoro-5-trifluoromethyl phenyl.

e) when X is a valence bond; $R^4$ is methyl; $R^3$ is hydrogen; and $R^2$ is cyano, then $R^1$ is not phenyl.

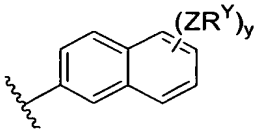
f) when X is a valence bond; $R^4$ is methyl; $R^2$ is $-(T)_nR$ wherein n is 0 and R is hydrogen; $R^3$ is hydrogen; and $R^1$ is $-(L)_mAr^1$ wherein m is 0; then $Ar^1$ is not 4-tolyl.

g) 2-[2,4-bis(1,1-dimethylpropyl)phenoxy]-N-[4-[1,6-dihydro-3-methyl-7-(4-nitrophenoxy)-6-oxo-5H-pyrazolo[4,3-c]pyridazin-5-yl]phenyl]-butanamide is excluded.

h) 2-[2,4-bis(1,1-dimethylpropyl)phenoxy]-N-[4-[5,6-dihydro-6-oxo-5-(2-pyridinyl)-1H-pyrazolo[4,3-c]pyridazin-3-yl]phenyl]-acetamide; and

N-[4-[5-(4-chlorophenyl)-5,6-dihydro-6-oxo-1H-pyrazolo[4,3-c]pyridazin-3-yl]phenyl]-2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]-butanamide are both excluded .

2. The compound according to claim 1, wherein $R^1$ is $-(L)_mAr^1$ and $Ar^1$ is selected from one of the following groups:



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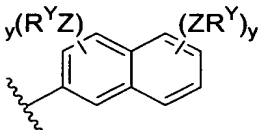

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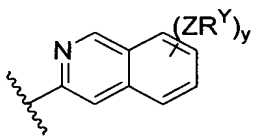

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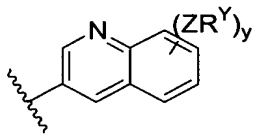

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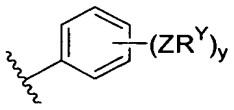

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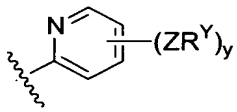

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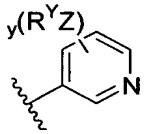

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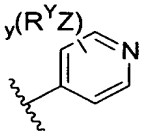

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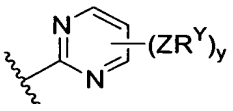

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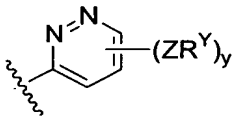

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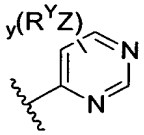

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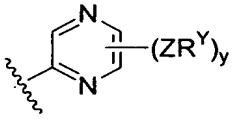

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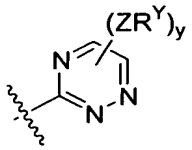

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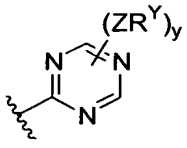

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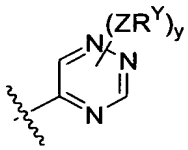

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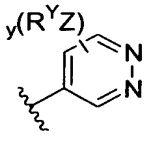

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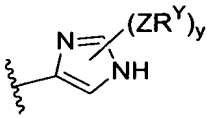

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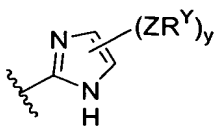

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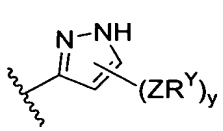

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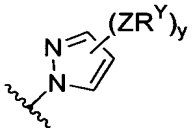

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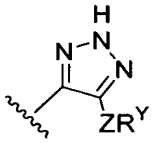

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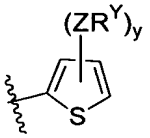

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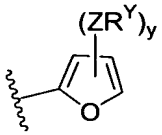

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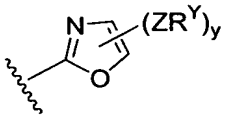

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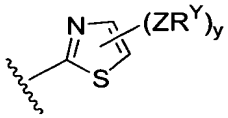

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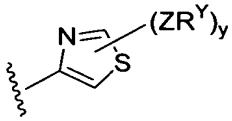

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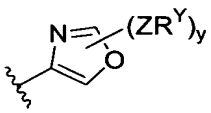

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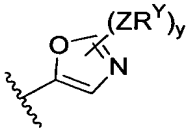

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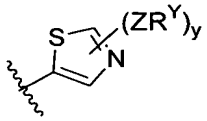

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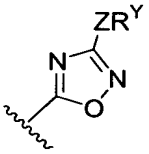

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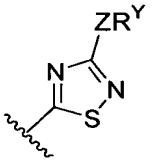

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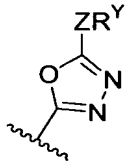

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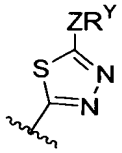

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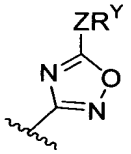

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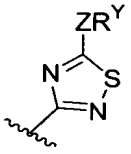
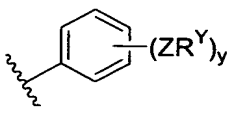
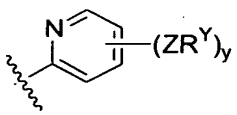


**1-36** .

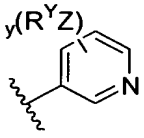
3. The compound according to claim 2, wherein $Ar^1$ is selected from one of the following groups:



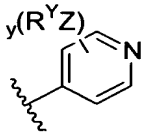
**1-5**



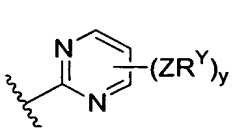
**1-6**



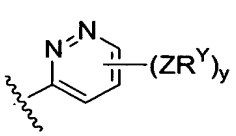
**1-7**



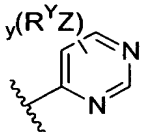
**1-8**



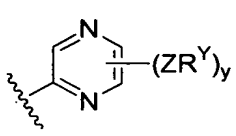
**1-9**



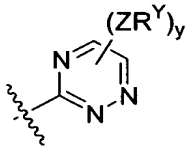
**1-10**



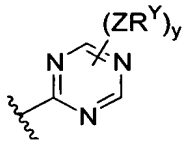
**1-11**



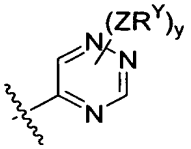
**1-12**



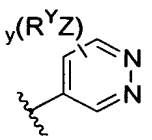
**1-13**



**1-14**

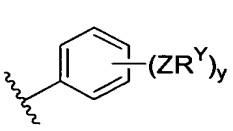


**1-15**

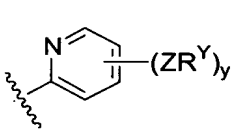


**1-16** .

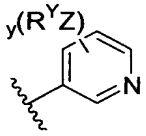
4. The compound according to claim 3, wherein $Ar^1$ is selected from one of the following groups:



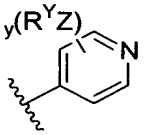
**1-5**



**1-6**

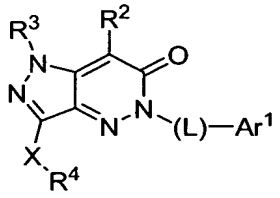


**1-7**



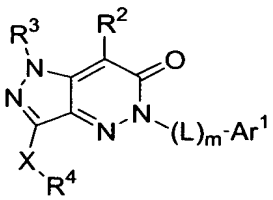
**1-8** .

5. The compound according to claim 2, wherein $R^1$ is $-(L)_m-Ar^1$, m is 1 and compounds have the formula **IA-3**:



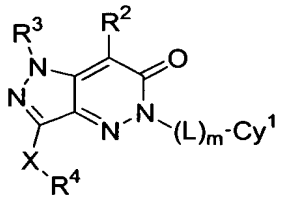
**IA-3** .

6. The compound according to claim 2, wherein $Ar^1$ is phenyl with 0-5 occurrences of $ZR^Y$ and compounds have the formula **IA-1-5**:



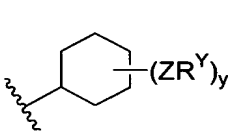
**IA-1-5** .

7. The compound according to claim 1, wherein $R^1$ is $-(L)_m-Cy^1$ and compounds have the formula **IA-2**:

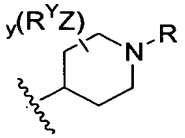


**IA-2**

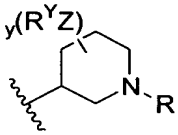
8. The compound according to claim 7, wherein $Cy^1$ is selected from one of the following groups:



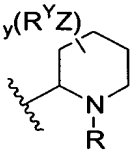
**2-1**



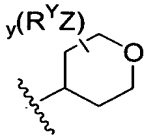
**2-2**



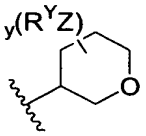
**2-3**



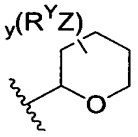
**2-4**



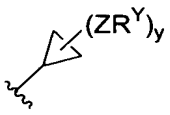
**2-5**



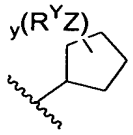
**2-6**



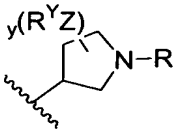
**2-7**



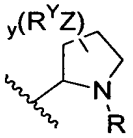
**2-8**



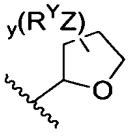
**2-9**



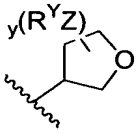
**2-10**



**2-11**



**2-12**



**2-13**

9. The compound according to claim 2, wherein L is an optionally substituted $C_{1-6}$ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, $NRCO_2$, CO, $CO_2$, CONR, CSNR, OC(O)NR, $SO_2$, $SO_2NR$, $NRSO_2$, $NRSO_2NR$, C(O)C(O), or $C(O)CH_2C(O)$ and m is 1.

10. The compound according to claim 9, wherein L is an optionally substituted $C_{1-6}$ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by CO, $CO_2$, CONR, CSNR, $SO_2NR$, and m is 1.

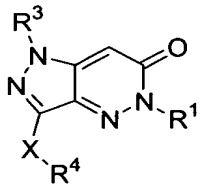
11. The compound according to claim 1, wherein $R^1$ is $-(L)_mR$, L is an optionally substituted $C_{1-6}$ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, $NRCO_2$, CO, $CO_2$, CONR, CSNR, OC(O)NR, $SO_2$, $SO_2NR$, $NRSO_2$, $NRSO_2NR$, C(O)C(O), or $C(O)CH_2C(O)$, R is an optionally substituted $C_{1-6}$ aliphatic group and m is 1.

12. The compound according to claim 1, wherein $R^2$ is selected from halogen, $NO_2$, CN, -SR, $-N(R)_2$, or $-(T)_nR$, wherein R is selected from hydrogen or an optionally substituted $C_{1-6}$ aliphatic group, or two R on the same nitrogen are taken together with the nitrogen to form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

13. The compound according to claim 12, wherein $R^2$ is selected from $-N(R)_2$, or $-(T)_nR$, wherein n is 0, and R is selected from hydrogen or an optionally substituted $C_{1-6}$ aliphatic group.

14. The compound according to claim 13, wherein $R^2$ is $-(T)_nR$, wherein n is 0, and R is selected from hydrogen, $CH_3$, or $CF_3$.

15. The compound according to claim 1, wherein $R^2$ is $-(T)_nR$, wherein n is 0, R is hydrogen, and compounds have the formula **IB**:

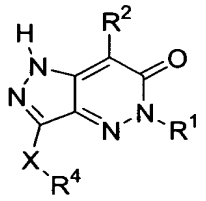


**IB**

16. The compound according to claim 1, wherein $R^3$ is hydrogen, methyl, ethyl, propyl, or isopropyl.

17. The compound according to claim 16, wherein $R^3$ is hydrogen or methyl.

18. The compound according to claim 1, wherein $R^3$ is hydrogen and compounds have the formula **IC**:

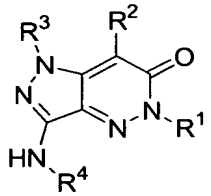


**IC**

19. The compound according to claim 1, wherein X is selected from a valence bond or NR.

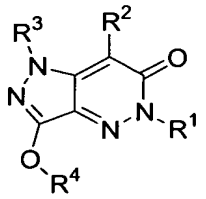
20. The compound according to claim 19, wherein X is NR and R is hydrogen.

21. The compound according to claim 1, wherein X is NR, R is hydrogen, and compounds have the formula **ID**:



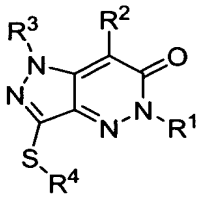
**ID**

22. The compound according to claim 1, wherein X is $OR^4$ and compounds have the formula **IE**:



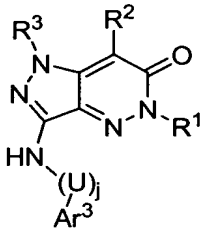
**IE**

23. The compound according to claim 1, wherein X is $SR^4$ and compounds have the formula **IF**:



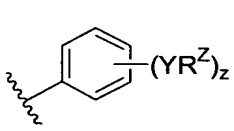
**IF**

24. The compound according to claim 1, wherein X is NR, R is hydrogen, $R^4$ is $-(U)_jAr^3$ and compounds have the formula **IG**:

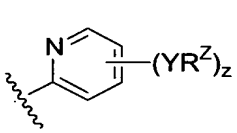


**IG**

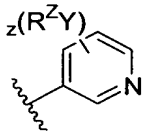
25. The compound according to claim 1, wherein $R^4$ is $-(U)_jAr^3$ and $Ar^3$ is selected from one of the following groups:



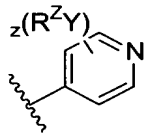
**1-5-a**



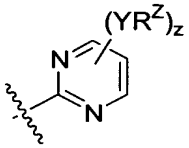
**1-6-a**



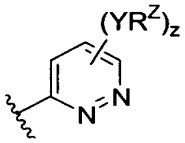
**1-7-a**



**1-8-a**

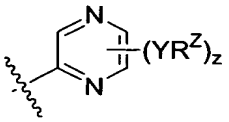


**1-9-a**

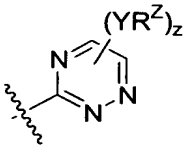


**1-10-a**

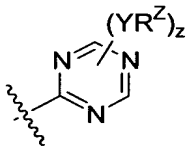
**1-11-a**



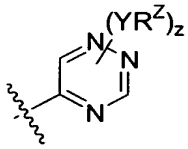
**1-12-a**



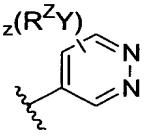
**1-13-a**



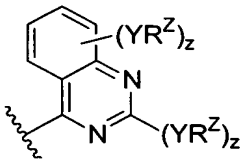
**1-14-a**



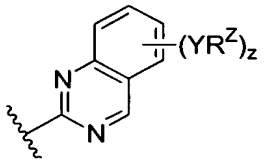
**1-15-a**



**1-16-a**

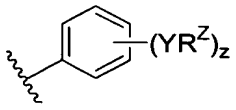


**1-37**

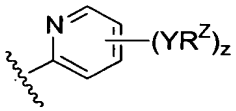


**1-38**

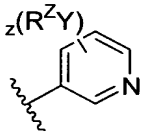
26. The compound according to claim 25, wherein $Ar^3$ is selected from one of the following groups:



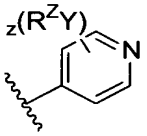
**1-5-a**



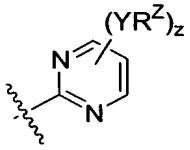
**1-6-a**



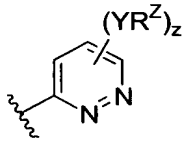
**1-7-a**



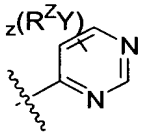
**1-8-a**



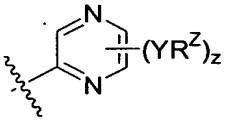
**1-9-a**



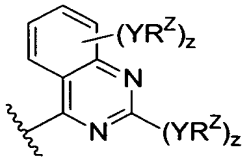
**1-10-a**



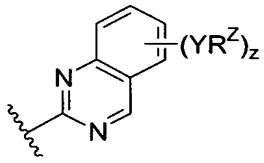
**1-11-a**



**1-12-a**

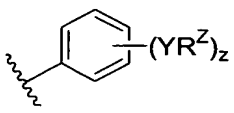


**1-37**

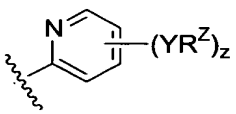


**1-38**

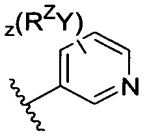
27. The compound according to claim 26, wherein $Ar^3$ is selected from one of the following groups:



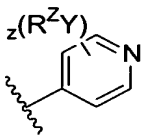
**1-5-a**



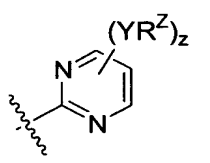
**1-6-a**



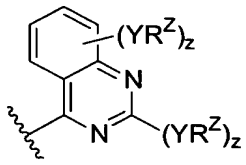
**1-7-a**



**1-8-a**

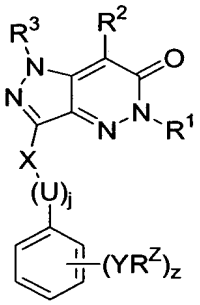


**1-9-a**

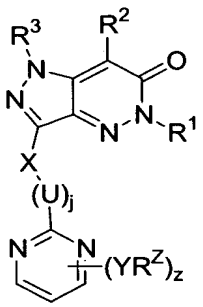


**1-37** .

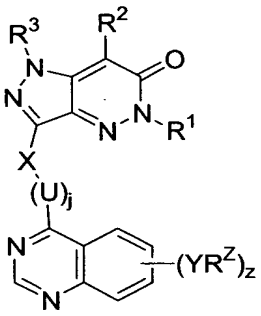
28. The compound according to claim 1, wherein $R^4$ is $-(U)_jAr^3$ and compounds have one of the following formulas:



**IE** .

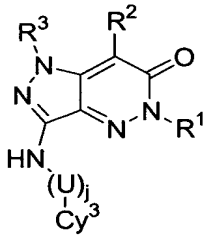


**IF**



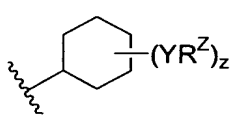
**IG** .

29. The compound according to claim 1, wherein X is NR, R is hydrogen, $R^4$ is $-(U)_jCy^3$ and compounds have the formula **IG-1**:



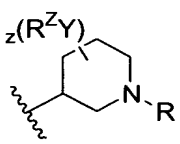
**IG-1** .

30. The compound according to claim 29, wherein $Cy^3$ is selected from one of the following groups:

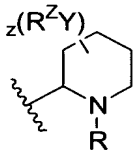


**2-1**

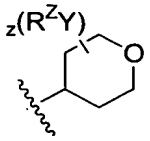
**2-2**



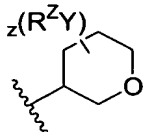
**2-3**



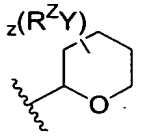
**2-4**



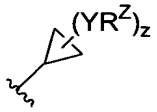

**2-5**



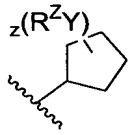

**2-6**



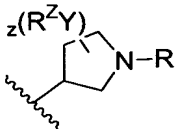

**2-7**



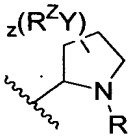

**2-8**



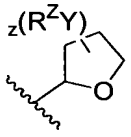

**2-9**



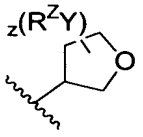

**2-10**




**2-11**

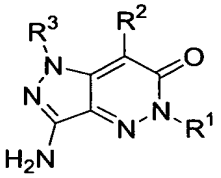



**2-12**



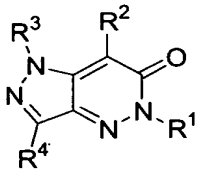

**2-13** .

31. The compound according to claim 1, wherein X is NR, R and $R^4$ are hydrogen, and compounds have the formula **IL**:




**IL** .

32. The compound according to claim 1, wherein X is a valence bond and compounds have the formula **IM**:




**IM** .

33. The compound according to claim 1, wherein $R^4$ is R and R is an optionally substituted $C_{1-6}$ aliphatic group.

34. The compound according to claim 1, wherein y is 0-5, and $Ar^1$ and $Cy^1$ are independently substituted with 0-5 occurrences of $ZR^Y$.

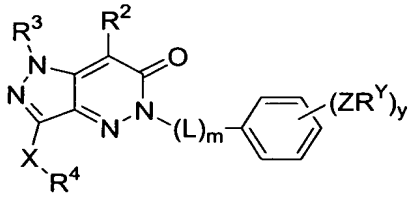
35. The compound according to claim 1, wherein y is 0-5, and $Ar^3$ and $Cy^3$ are independently substituted with 0-5 occurrences of $YR^Z$.

36. The compound according to claim 1, wherein y is 0, and $Ar^1$ is unsubstituted.

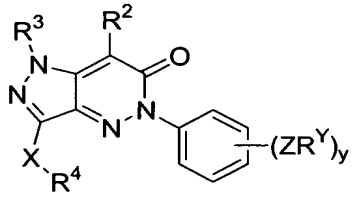
37. The compound according to claim 1, wherein $ZR^Y$ and $YR^Z$ groups are each independently halogen, $NO_2$, CN, or an optionally substituted group selected from $C_{1-4}$ aliphatic, aryl, aralkyl, $-N(R')_2$, $-CH_2N(R')_2$, -OR', $-CH_2OR'$, -SR', $-CH_2SR'$, -COOR', or $-S(O)_2N(R')_2$.

38. The compound of claim 30, wherein $ZR^Y$ and $YR^Z$ groups are each independently Cl, $CF_3$, $NO_2$, $-S(O)_2N(R')_2$ or an optionally substituted group selected from $C_{1-4}$ alkoxy, phenyl, phenyloxy, benzyl, or benzyloxy.

39. The compound according to claim 1, wherein $R^1$ is $-(L)_mAr^1$, m is 0 or 1, $Ar^1$ is phenyl optionally substituted with 0-5 occurrences of $ZR^Y$, and compounds have one of the following formulas **IIA** or **IIA-1**:

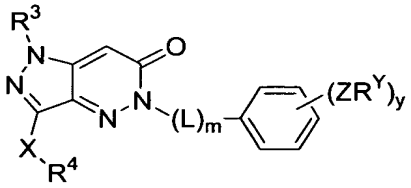


**IIA**

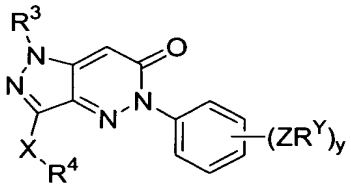


**IIA-1** .

40. The compound according to claim 1, wherein $R^2$ is $-(T)_nR$, wherein n is 0 and R is hydrogen, $R^1$ is $-(L)_mAr^1$, wherein m is 0 or 1, $Ar^1$ is phenyl optionally substituted with 0-3 occurrences of $ZR^Y$, and compounds have one of the following formulas **IIB** or **IIB-1**:

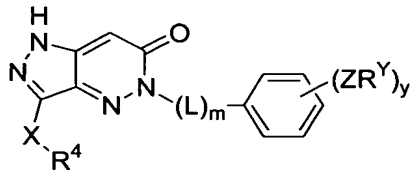


**IIB**

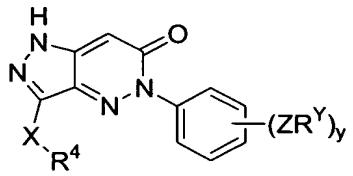


**IIB-1** .

41. The compound according to claim 1, wherein $R^2$ is $-(T)_nR$, wherein n is 0 and R is hydrogen, $R^3$ is hydrogen, $R^1$ is $-(L)_mAr^1$ wherein m is 0 or 1, $Ar^1$ is phenyl optionally substituted with 0-5 occurrences of $ZR^Y$, and compounds have one of the following formulas **IIC** or **IIC-1**:

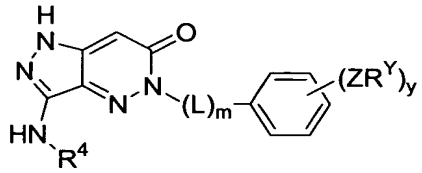


**IIC**

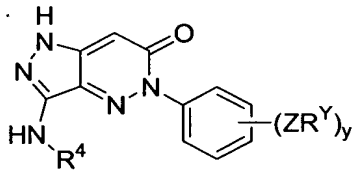


**IIC-1** .

42. The compound according to claim 1, wherein $R^3$ is hydrogen, $R^2$ is $-(T)_nR$, wherein n is 0 and R is hydrogen, X is NR, $R^1$ is $-(L)_mAr^1$ wherein m is 0 or 1, $Ar^1$ is phenyl optionally substituted with 0-5 occurrences of $ZR^Y$, and compounds have one of the following formulas **IID** or **IID-1**:

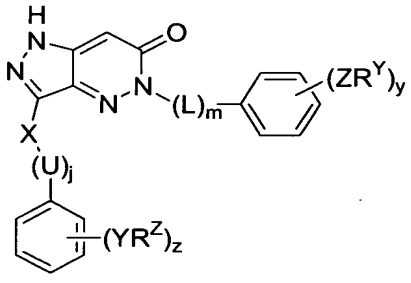


**IID**

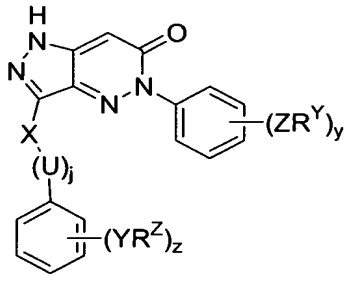


**IID-1** .

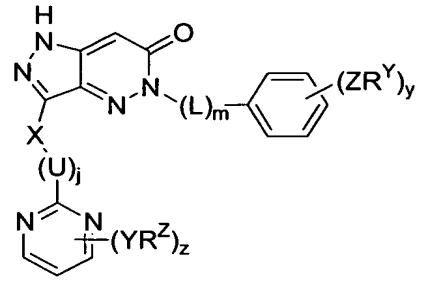
43. The compound according to claim 1, wherein $R^3$ is hydrogen, $R^2$ is $-(T)_nR$, wherein n is 0 and R is hydrogen, $R^1$ is $-(L)_mAr^1$ wherein m is 0 or 1, $Ar^1$ is phenyl optionally substituted with 0-5 occurrences of $ZR^Y$, and compounds have one of the following formulas **IIE, IIE-1, IIF, IIF-1, IIG,** or **IIG-1**:



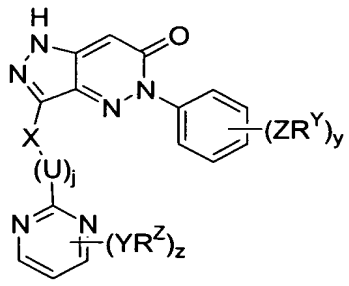
**IIE**



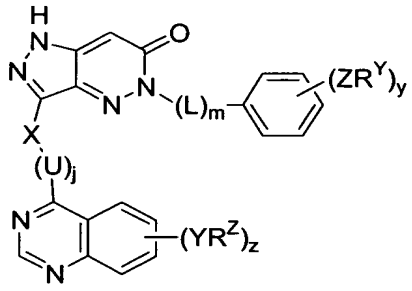
**IIE-1**



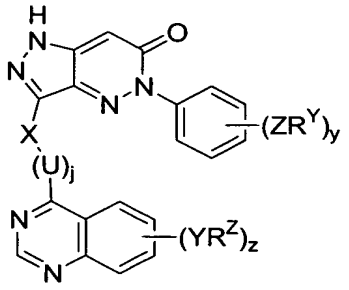
**IIF**



**IIF-1**

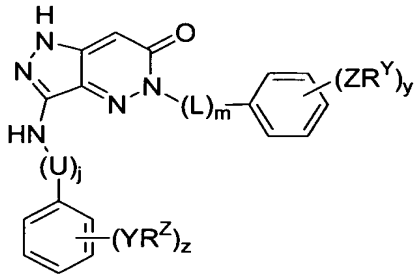


**IIG**

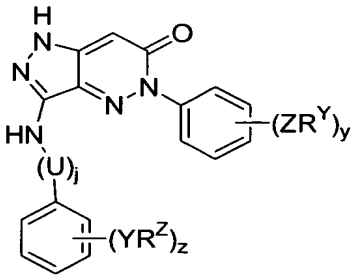


**IIG-1**

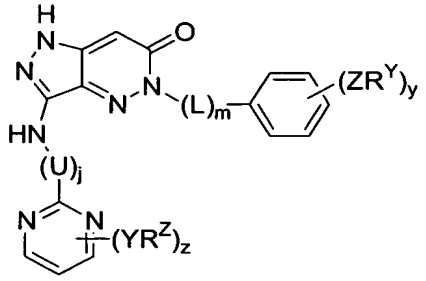
44. The compound according to claim 1, wherein $R^3$ is hydrogen, $R^2$ is $-(T)_nR$, wherein n is 0 and R is hydrogen, X is NH, $R^1$ is $-(L)_mAr^1$ wherein m is 0 or 1, $Ar^1$ is phenyl optionally substituted with 0-5 occurrences of $ZR^Y$, and compounds have one of the following formulas **IIIE, IIIE-1, IIIF, IIIF-1, IIIG, or IIIG-1**:



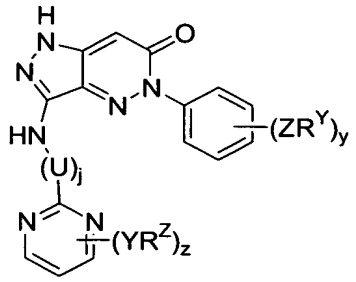
**IIIE**



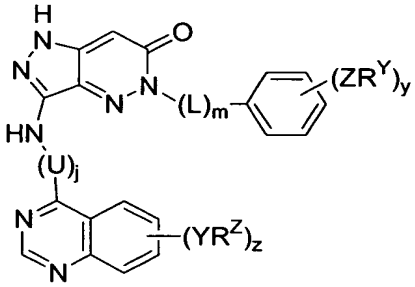
**IIIE-1**



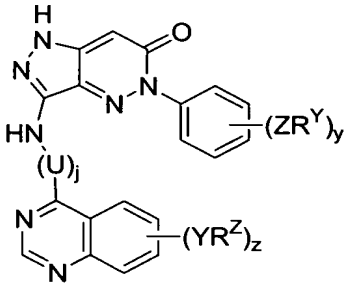
**IIIF**



**IIIF-1**

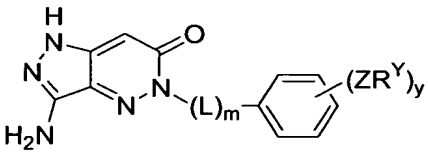


**IIIG**

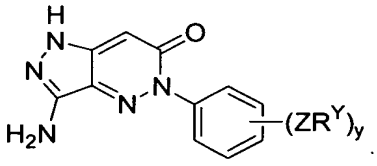


**IIIG-1**

45. The compound according to claim 1, wherein $R^3$ and $R^4$ are hydrogen, wherein $R^2$ is $-(T)_nR$, wherein n is 0 and R is hydrogen, X is NR, $Ar^1$ is optionally substituted phenyl, $R^1$ is $-(L)_mAr^1$, and compounds have one of the following formulas **IIH** or **IIH-1**:

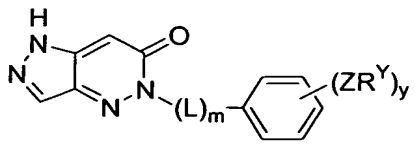


**IIH**

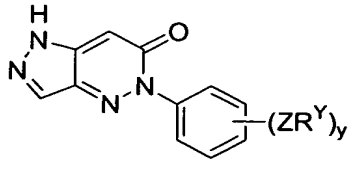


**IIH-1**

46. The compound according to claim 1, wherein $R^3$ and $R^4$ are hydrogen, wherein $R^2$ is $-(T)_nR$, wherein n is 0 and R is hydrogen, X is a valence bond, $Ar^1$ is optionally substituted phenyl, $R^1$ is $-(L)_mAr^1$, and compounds have one of the following formulas **IIJ** or **IIJ-1**:



**IIJ**



**IIJ-1**

47. The compound according to any one of claims 39-46, wherein $Ar^1$ is phenyl optionally substituted with 0-5 occurrences of $ZR^Y$ or wherein $Ar^1$ is pyridyl optionally substituted with 0-3 occurrences of $ZR^Y$.

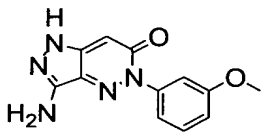
48. The compound according to claim 47, wherein m is 0 or m is 1 and L is $CH_2$; y is 0-3; and each occurrence of $ZR^Y$ is independently halogen, $NO_2$, CN, or an optionally substituted group selected from $C_{1-4}$ aliphatic, aryl, aralkyl, $-N(R')_2$, $-CH_2N(R')_2$, -OR', $-CH_2OR'$, -SR', $-CH_2SR'$, -COOR', or $-S(O)_2N(R')_2$.

49. The compound according to claim 48, wherein each occurrence of $ZR^Y$ is independently Cl, $CF_3$, $NO_2$, $-S(O)_2N(R')_2$ or an optionally substituted group selected from $C_{1-4}$ alkoxy, phenyl, phenyloxy, benzyl, or benzyloxy.

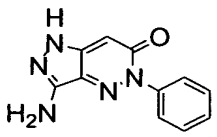
50. The compound according to any one of claims 24-28, wherein $Ar^3$ is phenyl or quinazolyl optionally substituted with 0-5 occurrences of $YR^Z$ or wherein $Ar^3$ is pyridyl or pyrimidinyl optionally substituted with 0-3 occurrences of $YR^Z$.

51. The compound according to claim 50, wherein j is 0 or 1 and U is $CH_2$; X is NH; m is 0 or 1 and L is $CH_2$; y is 0-3; and each occurrence of $YR^Z$ are each independently halogen, $NO_2$, CN, or an optionally substituted group selected from $C_{1-4}$ alkyl, aryl, aralkyl, $-N(R')_2$, $-CH_2N(R')_2$, -OR', $-CH_2OR'$, -SR', $-CH_2SR'$, -COOR', or $-S(O)_2N(R')_2$.

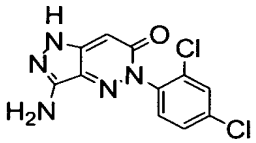
52. The compound according to claim 1, selected from one of the following compounds:



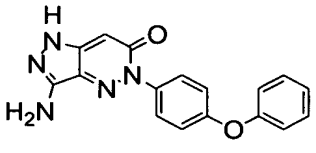
**I-1**



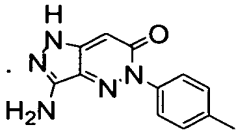
**I-2**



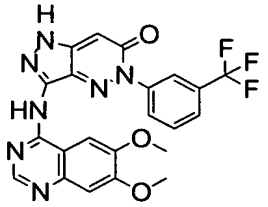
**I-3**



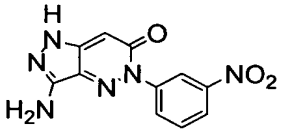
**I-4**



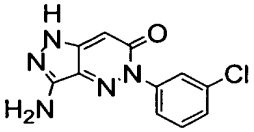
**I-5**



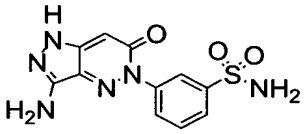
**I-6**



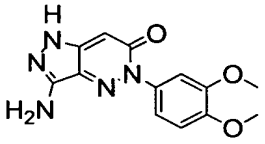
**I-7**



**I-8**



**I-9**



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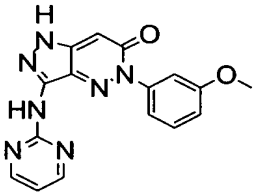
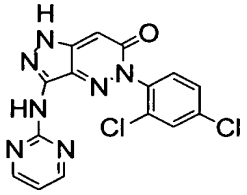
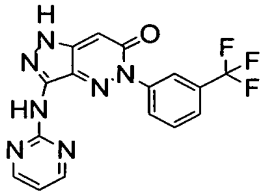


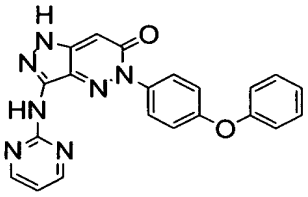
**I-11**



**I-12**



**I-13**



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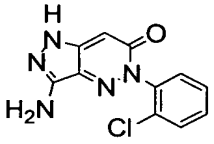
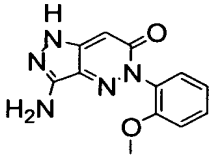
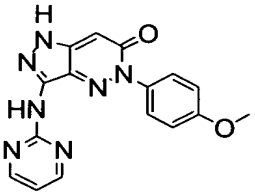


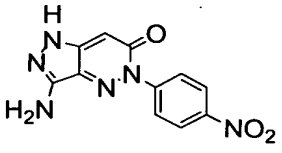
**I-15**



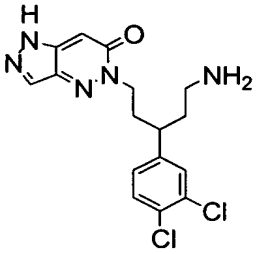
**I-16**



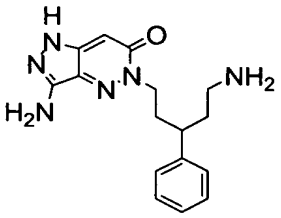
**I-17**



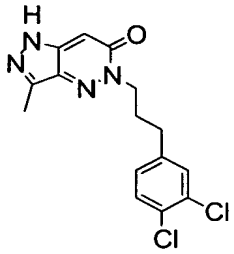
**I-18**



**I-19**



**I-20**



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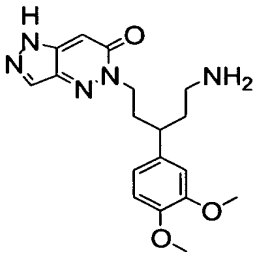
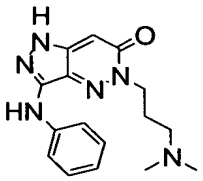


**I-22**



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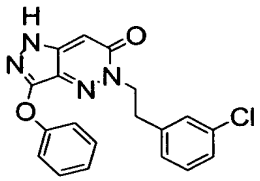

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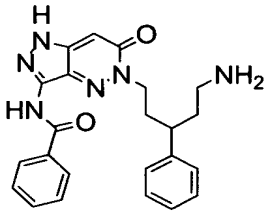

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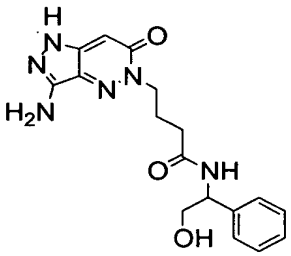
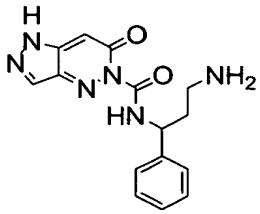
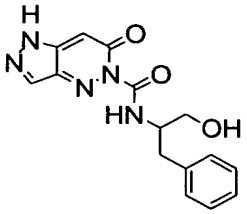


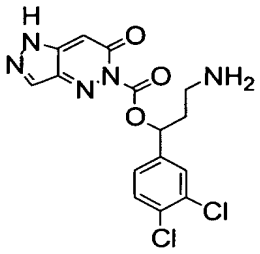
**I-26**



**I-27**



**I-28**



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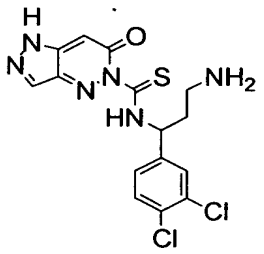
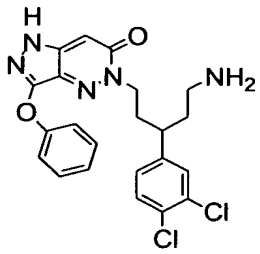
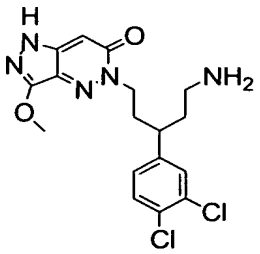


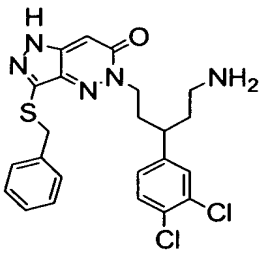
**I-30**



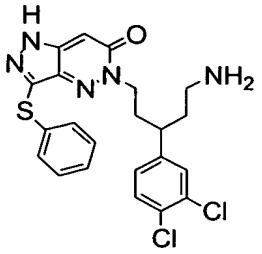
**I-31**



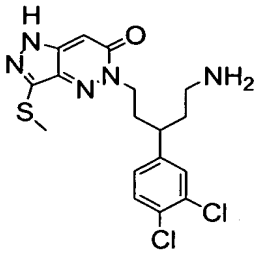
**I-32**



**I-33**



I-34



I-35

53. A pharmaceutically acceptable composition comprising a compound according to claim 1, and a pharmaceutically acceptable carrier, adjuvent, or vehicle.

54. The composition according to claim 53, additionally comprising an additional therapeutic agent selected from a treatment for Alzheimer's Disease (AD), a treatment for Parkinson's Disease, an agent for treating Multiple Sclerosis (MS), a treatment for asthma, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating stroke, an agent for treating cardiovascular disease, an antidepressant, an anti-psychotic agent, or an agent for treating diabetes.

55. A method of inhibiting GSK-3 kinase activity in a biological sample, comprising the step of contacting said biological sample with:

a) a composition according to claim 53; or

b) a compound according to claim 1.

56. A method of inhibiting GSK-3 kinase activity in a patient, comprising the step of administering to said patient:

a) a composition according to claim 53; or

b) a compound according to claim 1.

57. A method of treating an autoimmune disease, an inflammatory disease, a metabolic disorder, a psychiatric disorder, diabetes, an angiogenic disorder, tauopothy, a neurological or neurodegenerative disorder, a spinal cord injury, glaucoma, baldness, or a cardiovascular disease, in a patient in need thereof, comprising administering to said patient a composition according to claim 53.

58. The method according to claim 57, wherein said disease, disorder, or condition is selected from allergy, asthma, diabetes, Alzheimer's disease, Huntington's disease, Parkinson's disease, AIDS-associated dementia, amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease), multiple sclerosis (MS), an injury due to head trauma, schizophrenia, anxiety, bipolar disorder, tauopothy, a spinal cord or peripheral nerve injury, myocardial infarction, cardiomyocyte hypertrophy, glaucoma, attention deficit disorder (ADD), depression, a sleep disorder, reperfusion/ischemia, stroke, an angiogenic disorder, or baldness.

59. The method according to claim 58, wherein said disease, disorder, or condition is stroke.

60. The method according to claim 58, wherein said disease, disorder, or condition is Alzheimer's disease.

61. The method according to claim 57, wherein said disorder is a neurological or neurodegenerative disorder.

62. A method of decreasing sperm motility in a male patient comprising administering to said patient a composition according to claim 53.

63. The method according to claim 57, comprising the additional step of administering to said patient an additional therapeutic agent selected from a treatment for Alzheimer's Disease (AD), a treatment for Parkinson's Disease, an agent for treating Multiple Sclerosis (MS), a treatment for asthma, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating stroke, an agent for treating cardiovascular disease, an antidepressant, an anti-psychotic agent, or an agent for treating diabetes, wherein:

said additional therapeutic agent is appropriate for the disease being treated; and

said additional therapeutic agent is administered together with said composition as a single dosage form or separately from said composition as part of a multiple dosage form.